REMARKS

Claims 2 and 14 are amended to replace the general term "cognition deficit disorders" with the specific indications Alzheimer's Disease and attention deficit disorder, two of the three examples of cognition deficit diseases identified in the specification on page 2, lines 22-24, as particular disease targets for the compounds of the invention.

Claim 14 is also amended to specify the acetylcholinesterase inhibitors used in the combination treatment. Support for the list of cholinesterase inhibitors is found in the specification on page 28, lines 10-14.

In view of the restriction requirement, claim 15 has been canceled without prejudice to file a divisional application directed to that subject matter.

New claims 17 and 18 are added: new claim 17 is the same as claim 2, except that the fifth compound has been deleted, and new claim 18 corresponds to claim 14, but depends on new claim 17.

Claims 2 and 14 were rejected under 35 U.S.C. 112, first paragraph, for lack of enablement of the treatment of cognition deficit disorders; treatment of Alzheimer's Disease was considered enabled. Applicants urge that the treatment of attention deficit disorders is also enabled. A copy of Leurs et al, *TIPS*, *19* (1998), p. 177-183, is enclosed, wherein on page 181, the use of H_3 antagonists in the treatment of the attention deficit disorders is discussed. The instant specification refers to test procedures known in the art for determining H_3 antagonist activity on page 28, and Ki values for the specified compounds are shown on page 31. Similarly, m_2 antagonists have been widely reported to be useful in treating cognitive and learning disorders; see the background portions of the patents disclosing m_2 antagonist compounds incorporated by reference in the instant application.

Applicants have demonstrated the H_3 and m_2 antagonist activity of the compounds in claim 2, and H_3 antagonists and m_2 antagonists are separately known to improve cognitive deficits. In the absence of proof to the contrary, applicants urge that the claim that the dual H_3/m_2 antagonists listed in claim 2 are useful in treating Alzheimer's Disease and attention deficit disorder is not unreasonable or

unbelievable, and is enabled by the specification and/or the knowledge of those skilled in the art.

Claim 14 was rejected under 35 U.S.C. 112, first paragraph, for lack of enablement in not specifying the acetylcholinesterase inhibitors. Applicants urge that the amendment of claim 14 to include the acetylcholinesterase inhibitors listed in the specification overcomes this rejection.

Reconsideration and withdrawal of the rejections under 35 U.S.C. 112 are respectfully requested.

Claim 2 was rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al US 5,883,096 ('096). Applicants confirm that the subject matter of the various claims was commonly owned at the time the invention was made.

Although the rejection states that the '096 patent does not specifically teach the treatment of a cognition deficit, the reference is said to teach the method using di-N-substituted piperidines wherein the preferred compounds include the instant compound 5. The rejection states that the use of compound 5 to treat a cognition deficit would be obvious. Applicants point out that compound 5 of the present invention is not in the preferred scope of the '096 patent. The "R" group of the patent is the same as the corresponding portion of compound 5, as is the R^{29} group. However, the preferred R^1/R^{21} substitution in the patent comprises an alkyl, cycloalkyl or CN moiety at R^1, or R^1 and R^{21} together are =O or $=CH_2$, while in compound 5 the substitution corresponding to R^1/R^{21} is (H,H). Also, in the patent the preferred values for Y and Z are either N and N, or CH and N, respectively, while in compound 5 the corresponding atoms are N and CH (i.e., the preferred '096 compounds are 4-piperidinyl, while compound 5 is an N-piperidinyl). Since compound 5 is not within the preferred scope of the '096 patent (nor is it specifically disclosed), applicants respectfully submit that the use of compound 5 as a dual H_3 / m_2 antagonist is not rendered obvious by the '096 patent.

Applicants reiterate that since they are not claiming compounds per se, but rather a method of treatment comprising the administration of certain compounds, neither the novelty nor the obviousness of the compounds per se that are enumerated in claim 2 is an issue. While genuses of di-N-substituted piperidines are known as m2

muscarinic antagonists for treating cognition deficit disorders, there is no disclosure in '096, or in any publication known to applicants, that discloses that the m2 muscarinic antagonists also have activity as histamine H_3 receptor antagonists. Conversely, genuses of di-N-substituted piperidines are known as histamine H_3 receptor antagonists and there is disclosure of histamine H_3 receptor antagonists in the treatment of cognition deficit disorders, but there is no disclosure that such compounds have activity as m2 muscarinic antagonists. There is no motivation in the art to prepare and test the compounds listed in claim 2 for both m2 antagonist and H_3 antagonist activity for the treatment of cognition deficit disorders.

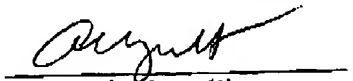
Claim 14 was rejected under 35 U.S.C. 103(a) as being unpatentable over an article in Drug Facts and Comparisons that teaches the use of tacrine to treat Alzheimer's Disease. The rejection states that it would be obvious to combine tacrine with compound 5 to treat cognition disorders. As discussed above, compound 5 is not within the scope of preferred compounds in the '096 patent, and applicants urge that since compound 5 is not obvious, the combinations with acetylcholinesterase inhibitors are not obvious.

Applicants claim the treatment of Alzheimer's Disease and attention deficit disorder with several specific novel compounds identified as dual H_3 / m_2 antagonists, and with combinations of those specific novel compounds and specific acetylcholinesterase inhibitors.

In particular, new claims 17 and 18, which do not include compound 5, are believed to overcome the rejections under 35 U.S.C. 103(a).

Reconsideration and withdrawal of the rejection of claim 2 under 35 U.S.C. 103(a) are respectfully requested.

Respectfully submitted,



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